A Retrospective Analysis of Pacritinib Treatment Outcomes in Myelofibrosis Patients With and Without Monocytosis

Eric Padron[1], Mrinal Patnaik[2], Daniel Wiseman[3], Raphael Itzykson[4], Douglas Tremblay[5], John Mascarenhas[5], Sarah Buckley[6], Karisse Roman-Torres[6], Michael R. Savona[7]

[1]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA; [2]Mayo Clinic, Rochester, MN, USA; [3]University of Manchester, Manchester, England, UK; [4]Service Hématologie Adultes, INSERM/CNRS UMR 944/7212, Hôpital Saint-Louis, France; [5]Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA; [6]Sobi Inc., Waltham, MA, USA; [7]Vanderbilt-Ingram Cancer Center, Vanderbilt University School of Medicine, Nashville, TN, USA.

Conclusions

- While monocytosis in myelofibrosis (MF) is not a cardinal finding, it is present in a sizable minority of patients and is a known predictor of poor outcomes in MF. By contrast, outcomes with pacritinib do not appear inferior in MF patients with monocytosis compared with those without
- Given this, and the dire need for new therapies for chronic myelomonocytic leukemia (CMML), particularly the proliferative type (MP-CMML), these data provide rationale to study pacritinib in patients with CMML, which is actively being planned

Background

- While sustained monocytosis has been described as a high-risk feature in patients with MF,[1] it is also a core diagnostic component for CMML
- The presence of driver mutations such as JAK2V617F, bone marrow fibrosis, and extramedullary hematopoiesis can be seen in both entities
- Pacritinib is a JAK2 inhibitor approved for MF, and also has potency in the inhibition of CSF1R and IRAK1,[2] both of which are kinases upregulated in CMML
- While pacritinib has not yet been tested in CMML, it has shown preclinical activity in murine CMML models[3]
- As MF and CMML occur along a clinical spectrum, treatment outcomes in patients with MF with monocytosis might inform therapies in CMML

Aim

- To retrospectively analyze clinical outcomes of MF patients with versus without monocytosis treated with pacritinib across two phase 3 studies (PERSIST-1 and PERSIST-2)

Methods

- Patients treated with pacritinib on the PERSIST-1 (JAK inhibitor-naïve) and PERSIST-2 (JAK inhibitor-naïve or ruxolitinib refractory with platelets ≤100 × 10^9/L) trials were included
- Patients were stratified based on the presence (≥10% monocytes and absolute monocyte count ≥0.5 × 10^9/L) or absence of baseline monocytosis
- Week 24 efficacy outcomes were analyzed in the intention-to-treat-efficacy population randomized ≥22 weeks prior to study termination and included spleen volume reduction (SVR), Total Symptom Score (TSS) response, and Patient Global Impression of Change (PGIC)
- Only patients who completed the Myeloproliferative Neoplasm-Symptom Assessment Form (MPN-SAF) TSS version 2.0 were included
- Transfusion independence response (TI-R) was assessed among patients requiring red blood cell (RBC) transfusion at baseline (assessed within 90 days prior to baseline), with response defined as the absence of RBC transfusions over any 12-week period through 24 weeks (Gale criteria)
- Change in hemoglobin and monocytes over time was determined for those patients with monocytosis
- Data are summarized using descriptive statistics such as mean, median and quartiles for continuous endpoints and count and percent for categorical endpoints

Results

Baseline Characteristics

- At baseline, 35 patients (8%) had monocytosis and 395 patients did not
- The two groups were similar in age, sex, JAK inhibitor-naïve, and JAK2V617F-positive (**Table 1**)
- Median white blood cell count was higher in patients with monocytosis than those without, while median platelet count was lower in patients with monocytosis compared with those without (**Table 1**)

Table 1. Patient Characteristics

Baseline characteristics	Patients with monocytosis N=35	Patients without monocytosis N=395
Age, median years	70	67
Males, n (%)	22 (62.9)	218 (55.2)
DIPSS high risk, n (%)	10 (28.6)	81 (20.5)
Platelet count, × 10^9/L, median	64	89
Hemoglobin, g/dL, median	9.7	10.0
WBC, × 10^9/L, (median, IQR)	11.8 (6.0, 32.4)	8.9 (4.8, 20.0)
JAK-inhibitor naïve, n (%)	23 (65.7)	304 (77.0)
JAK2V617F-positive, n (%)	26 (74.3)	288 (72.9)
Spleen length, cm, median	13	13
Spleen volume, cm^3, median	2662.9	2167.3

DIPSS, Dynamic International Prognostic Scoring System; IQR, interquartile range; JAK, Janus kinase; WBC, white blood cell.

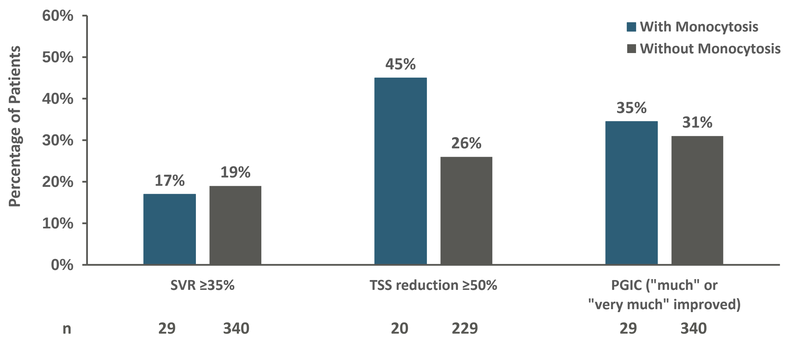
Treatment Duration

- Average treatment duration was 9.75 months for patients with monocytosis and 11 months for those without

Similar Efficacy With and Without Monocytosis

- The percentage of patients achieving SVR ≥35% and PGIC responses of "much" and "very much" improved at week 24 were similar between the groups (**Figure 1**)
- TSS response rate in patients with monocytosis was numerically higher (P=0.103)

Figure 1. Percentage of Patients Achieving Efficacy Outcomes



SVR, spleen volume reduction; TSS, total symptom score (version 2.0, excluding tiredness); PGIC, Patient Global Impression of Change.

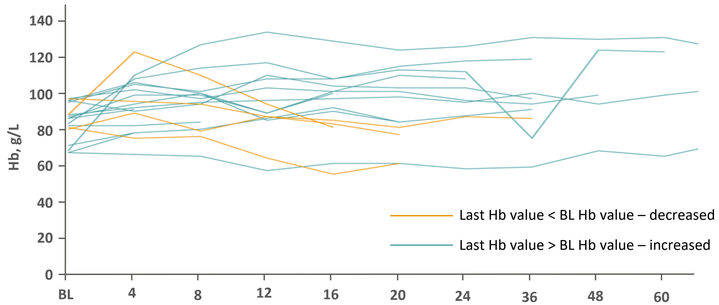
Median Reduction of Spleen Volume and Symptom Burden

- The median SVR was similar in those with (19%) and without monocytosis (23%)
- The median reduction in TSS was 55% in those with monocytosis versus 35% in those without monocytosis

Anemia Benefit in Patients with Monocytosis

- Among the 16 patients on pacritinib with monocytosis who received RBC transfusions at baseline, 50% (n=8) of patients also achieved TI-R
- Among the 34 patients on pacritinib with monocytosis and who had hemoglobin <10 g/dL at baseline, 22.2% of patients had an increase of 1.5 g/dL of hemoglobin and 11.1% had ≥2 g/dL increase
- Many of the patients with monocytosis on pacritinib (14 /18) experienced stabilization or an increase in hemoglobin levels over time (**Figure 2**)

Figure 2. Change in Hemoglobin Over Time for Patients with Monocytosis



BL, baseline; Hb, hemoglobin.

Reduction of Monocytes with Pacritinib

- Median percent change from baseline to week 24 for absolute monocyte count in the pacritinib-treated patients with monocytosis (n=16) was -72.5 (interquartile range: -87.3, -0.2)

Safety

- The rates of treatment-emergent serious adverse events (~50% in each group) and treatment-emergent adverse events leading to drug discontinuation (26% in those with vs 20% without monocytosis) were not significantly different between groups, suggesting no safety signal specific to the presence of monocytosis

References

1. Teferi A, et al. *Br J Haem* 2018;812–845; **2.** Singer JW, et al. *J Exp Pharmacol* 2016;8:11–19; **3.** Yoshimi A, et al. *Blood* 2017;130:397–407.

Acknowledgements

The study is funded by CTI BioPharma Corp, a Sobi company. The authors wish to acknowledge the contribution of the study participants, investigators and their teams. The authors also acknowledge Kathleen York CMPP from Sobi for publication coordination and Purvi Suthar, PharmD from Sobi for medical writing assistance. This poster was created by the authors in accordance with Good Publication Practice (GPP) 2022 guidelines (https://www.ismpp.org/gpp-2022). Editorial assistance, funded by Sobi, was provided by Linda Buss PhD and Blair Hesp PhD CMPP of Kainic Medical Communications Ltd. (Dunedin, New Zealand). Sobi reviewed and provided feedback on the poster. The authors had full editorial control of the poster and provided their final approval of all content. This poster was previously presented at the EHA2024 Hybrid Congress, June 13–16, 2024 in Madrid, Spain and online.

Disclosures

EP: Advisory Board: CTI BioPharma Corp, a Sobi company; **MP:** Research Funding: Kura Oncology, Stem Line Pharmaceuticals, Epigenetix, Solu therapeutics, Polaris; Advisory Board: CTI BioPharma Corp, a Sobi company; **DW:** Consultancy: CTI BioPharma Corp, a Sobi company, **RI:** None; **DT:** Research Funding: CTI BioPharma Corp, a Sobi company; **JM:** Consultancy: Abbvie, CTI BioPharma Corp, a Sobi company, Geron, GlaxosSmithKline, Imago, Incyte, Celgene, BMS, Kartos, Kayropharm, MorphoSys, Novartis, Pfizer, PharmaEssentia, Sierra; Research Funding: Abbvie, BMS, Celgene, CTI BioPharma Corp, a Sobi company, Geron, Incyte, Novartis, Kartos, PharmaEssentia; **SB, KRT:** are employed by Sobi Inc. and have received payment of unvested equity awards from CTI BioPharma Corp., a Sobi company, following its acquisition in June 2023 by the Swedish Orphan Biovitrum AB (publ); **MS:** Advisory Board: CTI BioPharma Corp, a Sobi company.

For additional information contact: Dr. Eric Padron: eric.padron@moffitt.org